

# Long-Term Outcome Following Surgery for Colorectal Cancers in Octogenarians: A Single Institution's Experience of 204 Patients

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## Abstract

**Background** The incidence of colorectal cancer in elderly patients is likely to increase with an aging population. The aims of this study are to review our experience in the surgical management of octogenarians with colorectal cancers and to identify factors that influence the short-term and long-term outcomes.

**Methods** A retrospective review of all octogenarians who underwent surgery for colorectal cancer from December 2002 to October 2008 was performed.

**Results** We identified 204 patients with a median age of 84 years (range, 80–97 years). The majority of patients had an American Society of Anesthesiologists score  $\geq 3$  ( $n=142$ , 69.6%) and a Charlson Comorbidity Index of  $\leq 3$  ( $n=128$ , 62.7%). Emergency surgery was performed in 83 (40.7%) patients. Left-sided malignancy was seen in 138 patients (67.6%). Most of the patients had either stage II ( $n=75$ , 36.8%) or III ( $n=69$ , 33.8%) diseases. The 30-day mortality rate was 16.2% ( $n=33$ ). After multivariate analysis, the independent variables predicting worse perioperative complications and death were age  $>85$  years old, emergency surgery, and Charlson Comorbidity Index  $>3$ . The median follow-up for the 171 remaining patients was 27 months (range, 2–92 months). The 30-day readmission rate was 2.9% ( $n=5$ ). Thirty-one (21.2%) of 146 patients who survived curative surgery developed recurrent disease. Seventy (34.3%) patients died from various etiologies after their first 30 days postoperatively (60% cancer-specific with median survival of 15 months and 40% noncancer-related with median survival of 14 months). Overall and disease-free survivals were adversely affected in patients with advanced malignancy and in those with severe perioperative complications.

**Conclusions** Surgery for octogenarians with colorectal cancers is associated with significant morbidity and mortality rates which are associated with advanced age, emergency surgery, and Charlson Comorbidity Index  $>3$ . Long-term survival is dependent on the stage of the malignancy and the presence of severe perioperative complications.

**Keywords** Octogenarian · Elderly · Colorectal · Cancer · Surgery · Treatment outcome

## Introduction

The incidence of colorectal cancer in elderly patients is likely to increase worldwide with increasing life expectancy.<sup>1–3</sup>

Despite the advances in surgical techniques and improvements in anesthetic procedure and intensive care, the perioperative complications in these high-risk patients are still considerable.<sup>1–5</sup> Recent studies have demonstrated comparable long-term outcome in elderly patients to younger patients following curative surgical resection for malignancy of similar stage, albeit with higher complication rates.<sup>4–8</sup> It is not entirely clear if age alone or its associated comorbidities or other factors account for these outcomes.

In view of all the above issues, we undertook this study with the primary aim to identify the factors that could influence the short-term and long-term outcomes in octogenarians undergoing surgery for colorectal cancers.

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## Methods

### Study Population

A retrospective review of all patients aged 80 years and older who underwent operative intervention for colorectal malignancy from December 2002 to October 2008 was performed. Patients were identified from the hospital's diagnostic index and operating records and all malignancies were confirmed by histological evaluation. Right-sided pathology was regarded if it was located from the cecum till the transverse colon, while left-sided pathology commenced from the splenic flexure.

The data collected included age, gender, American Society of Anesthesiologists (ASA) score, and comorbid conditions. The Charlson Comorbidity Index (Table 1) was used to better determine the severity of the comorbidities in this group of patients. Laboratory values, including full blood count and renal panel, were also recorded. In addition, operative findings and interventions, perioperative complications, mortality, and length of hospital stay were also documented.

Curative resection was defined as the complete excision of the primary tumor and its locoregional lymph nodes in stages I–III disease, while palliative surgery would indicate the presence of residual tumor at the primary and/or distant site/s and thus would include nonresectional bypass or diversion stoma. All colorectal cancers were staged according to the guidelines of the American Joint Committee of

Cancer. The grades of complications (GOC) were in concordance to the classification proposed by Clavien and group<sup>9–11</sup> (Table 2).

Disease recurrence was diagnosed after radiological and/or pathological evaluation. The overall survival duration was documented from the date of surgery until the date of death. Our institution's routine follow-up protocol for any patient with resected colorectal malignancy included 3-monthly review with carcinoembryonic antigen (CEA) levels for the first 2 years followed by 6-monthly review with CEA levels for the subsequent 3 years. Surveillance colonoscopy would be performed 1 year after any oncologic resection. Postoperative computed tomographic scan of the thorax, abdomen, and pelvis is not routinely performed. It would be performed only if there was a high index of suspicion of recurrence or for monitoring of the response of metastatic disease following chemotherapy.

Statistical analysis was performed using both univariate and multivariate analyses. The variables were analyzed to the various outcomes using the Fisher's exact test, and their odds ratio (OR) and 95% confidence interval (95% CI) were also reported. For the multivariate analysis, the logistic regression model was applied. The overall survival probability, excluding operative mortality, was estimated according to the Kaplan–Meier method, and the Cox multivariate analysis would be performed to identify independent factors for disease-free and overall survival. All analyses were performed using the SPSS 17.0 statistical package (Chicago, IL, USA) and all *p* values reported are two-sided, and *p* values of <0.05 were considered statistically significant.

**Table 1** Charlson Comorbidity Index

Comorbid condition	Score
Myocardial infarct	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Ulcer disease	1
Mild liver disease	1
Diabetes	1
Hemiplegia	2
Moderate or severe renal disease	2
Diabetes with end-organ damage	2
Any tumor	2
Leukemia	2
Lymphoma	2
Moderate or severe liver disease	3
Metastatic solid tumor	6
AIDS	6

## Results

During the study period, a total of 1,415 patients with colorectal cancers underwent related surgeries in our institution. Of these, 204 (14.4%) patients with a median age of 84 years (range, 80–97 years) formed the study group. The majority of these patients had an ASA score  $\geq 3$  ( $n=142$ , 69.6%).

**Table 2** Classification of surgical complications<sup>9–11</sup>

GOC
Grade I: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
Grade II: Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
Grade III: Requiring surgical, endoscopic, or radiological intervention
Grade IV: Life-threatening complication(s) requiring ICU management (including organ dysfunction)
Grade V: Death of a patient

Hypertension, diabetes mellitus, and ischemic heart disease were present in 127 (62.3%), 50 (24.5%), and 47 (23.0%) patients, respectively. The median Charlson Comorbidity Index was 3 (range, 2–10), with a majority of them having a score of  $\leq 3$  ( $n=128$ , 62.7%). Emergency surgery was performed in 83 (40.7%) patients for various indications such as obstruction ( $n=62$ , 74.7%), perforation ( $n=13$ , 15.7%), and inflammatory mass ( $n=8$ , 9.6%). Left-sided malignancy was present in 138 patients (67.6%), with the sigmoid colon being the most frequently involved site in 54 (26.5%) patients. There were six (2.0%) patients with synchronous colonic malignant lesions. In the 37 patients with rectal cancer, none underwent neoadjuvant chemoradiation therapy. Table 3 illustrates the characteristics of the study group.

Operative Findings

Right hemicolectomy, anterior resection, and Hartmann’s procedure were performed most frequently in 61 (29.9%), 51 (25.0%), and 45 (22.1%) patients, respectively. Most of the patients ( $n=187$ , 91.7%) underwent open surgery. Stoma

was created in 94 (46.1%) patients, while curative resection was performed in 164 (80.4%) patients. There were 75 (36.8%) and 69 (33.8%) patients with stage II and III diseases, respectively. Thirty-one (15.2%) patients already had metastatic disease on diagnosis. Table 4 highlights the surgical findings and procedures of the study group.

The 30-day mortality rate of our series was 16.2% ( $n=33$ ), while another 39 (19.1%) patients had severe perioperative complications (GOC III and IV; Table 5). Anastomotic leak and wound dehiscence were seen in six (5.5%) and seven

**Table 3** Characteristics of the study group

	Number (percent)
Median age, range (years)	84 (80–97)
$\leq 85$	133 (65.2)
$> 85$	71 (34.8)
Gender	
Male	86 (42.2)
Female	118 (57.8)
Urgency of surgery	
Elective	121 (59.3)
Emergency	83 (40.7)
ASA score	
1	0
2	62 (30.4)
3	129 (63.2)
4	13 (6.4)
Premorbid condition	
Hypertension	127 (62.3)
Diabetes mellitus	50 (24.5)
Hyperlipidemia	53 (26.0)
Ischaemic heart disease	47 (23.0)
History of cerebrovascular accident	40 (19.6)
Number of premorbid condition	
0–1	103 (50.5)
$> 1$	101 (49.5)
Median Charlson Comorbidity index	3 (2–10)
0–3	128 (62.7)
$>$	76 (37.3)

**Table 4** Surgical observations and procedures of the study group

	Number (percent)
Site of malignancy	
Right-sided	60 (29.4)
Cecum	20 (9.8)
Ascending colon	18 (8.8)
Hepatic flexure	11 (5.4)
Transverse colon	11 (5.4)
Left-sided	138 (67.6)
Splenic flexure	12 (5.9)
Descending colon	15 (7.4)
Sigmoid colon	54 (26.5)
Rectosigmoid	20 (9.8)
Rectum	37 (18.1)
Synchronous lesions	6 (2.9)
Laparoscopic procedure	12 (5.9)
Laparoscopic converted open	5 (2.5)
Open procedure	187 (91.7)
Surgery performed	
Right hemicolectomy	61 (29.9)
Anterior resection with defunctioning stoma	35 (17.2)
Anterior resection without defunctioning stoma	16 (7.8)
Hartmann’s procedure	45 (22.1)
Defunctioning stoma only without resection	14 (6.9)
Subtotal/total or panproctocolectomy	13 (6.4)
Left hemicolectomy	8 (3.9)
Abdominoperineal resection	5 (2.5)
Sigmoid colectomy	4 (2.0)
Segmental resection	2 (1.0)
Ileocolic bypass	1 (0.5)
Creation of stoma	
Yes	94 (46.1)
No	110 (53.9)
Stage of malignancy	
Stage I	20 (9.8)
Stage II	75 (36.8)
Stage III	69 (33.8)
Stage IV	31 (15.2)
Unknown	9 (4.4)

**Table 5** Perioperative outcome of the study group

	Number (percent)
GOC	
No complications	50 (24.5)
Grade I	27 (13.2)
Grade II	55 (27.0)
Grade III	11 (5.4)
Grade IV	28 (13.7)
Death or grade V	33 (16.2)
Specific complications	
Anastomotic leak	6 (2.9)
Wound dehiscence	7 (3.4)
Relook laparotomy	13 (6.4)
Median length of stay (days)	11 (1–130)

(3.4%) patients, respectively. Thirteen (6.4%) patients underwent relook laparotomy. The median length of stay was 11 days (range, 1–130 days).

The independent factors that were associated with worse perioperative outcome (GOC III–V) included Charlson Comorbidity Index >3, age >85 years, and emergency surgery (Table 6). Factors such as ASA score, location of pathology, renal impairment, and stoma creation were not associated with worse outcome after multivariate analysis

#### Follow-up

A total of 171 patients survived surgery and were discharged well. The majority of them ( $n=119$ , 69.6%) were discharged home, while 52 (30.4%) patients were sent to step-down care for further rehabilitation. These patients were followed up for a median period of 27 months (range, 2–92 months). The 30-day readmission rate was 2.9% ( $n=5$ ). Around 75%

( $n=128$ ) of them were readmitted a total of 221 times for various nonsurgical (135 admissions) and surgical-related (86 admissions) causations. Of the patients who had a stoma ( $n=94$ ) created, only three patients with ileostomy and one patient with end colostomy had it closed or reversed.

There were only 17 patients who underwent adjuvant chemotherapy. The remaining patients either declined or were not offered by the medical oncologists due to their advanced age or significant comorbid conditions. In the 146 patients who had curative resection and survived the initial surgery, 31 (21.2%) developed recurrent disease. The recurrences were diagnosed at a median duration of 12 months (range, 3–50 months) from the surgery. The majority of the recurrences involved distant organs such as the liver ( $n=16$ ), lung ( $n=11$ ), and peritoneum ( $n=10$ ). There were six patients who developed local recurrences, four of whom already have systemic disease then. The only two patients with isolated local recurrences were scheduled for further operations (anterior resection) to remove their local recurrences. Unfortunately, one had incidental peritoneal metastasis diagnosed intraoperatively and passed away 6 months later. The other patient underwent a successful reoperation and is still currently well with no evidence of recurrence.

Not surprisingly, the majority ( $n=21$ , 67.7%) of the patients who developed recurrent disease had stage III disease initially. After multivariate analysis, the independent factors associated with disease recurrence included stage III disease (OR, 3.74; 95% CI, 1.61–8.71), emergency surgery (OR, 2.90; 95% CI, 1.29–6.54), and the presence of severe complications (GOC III and IV) (OR, 2.57; 95% CI, 1.07–6.15).

#### Survival

Seventy (34.3%) patients died subsequently, with a majority of them ( $n=42$ , 60.0%) due to the underlying malignancy (Table 7). The median duration of survival was 15 months

**Table 6** Analysis of variables associated with worse perioperative outcome (including death)

Characteristics	GOC 0–II ( $n=132$ )	GOC III–V ( $n=72$ )	OR (95% CI)	<i>p</i> value
>85 years old	37 (28.0%)	34 (43.6%)	2.30 (1.26–4.18)	0.009 <sup>a</sup>
Emergency surgery	42 (31.8%)	41 (43.6%)	2.83 (1.57–5.13)	0.001 <sup>a</sup>
ASA score 3–4	84 (63.6%)	58 (79.5%)	2.37 (1.20–4.69)	0.016
≥1 premorbid conditions	67 (50.8%)	34 (53.8%)	0.87 (0.49–1.54)	>0.05
Charlson Comorbidity Index >3	36 (27.3%)	40 (56.4%)	3.33 (1.83–6.10)	<0.001 <sup>a</sup>
WBC >10.0	48 (36.4%)	28 (46.2%)	1.11 (0.62–2.01)	>0.05
Hct (<33.0) (%)	71 (53.8%)	41 (46.2%)	1.14 (0.64–2.03)	>0.05
Serum urea >9.3 (mmol/L)	19 (14.4%)	20 (25.6%)	2.29 (1.13–4.65)	0.025
Serum creatinine >110 (μmol/L)	28 (21.2%)	28 (33.3%)	2.36 (1.26–4.44)	0.009
Metastatic disease	13 (9.8%)	18 (17.9%)	3.05 (1.40–6.67)	0.007
Left-sided pathology	91 (68.9%)	52 (64.1%)	1.17 (0.62–2.21)	>0.05
Creation of stoma	51 (38.6%)	43 (53.8%)	2.36 (1.31–4.24)	0.005

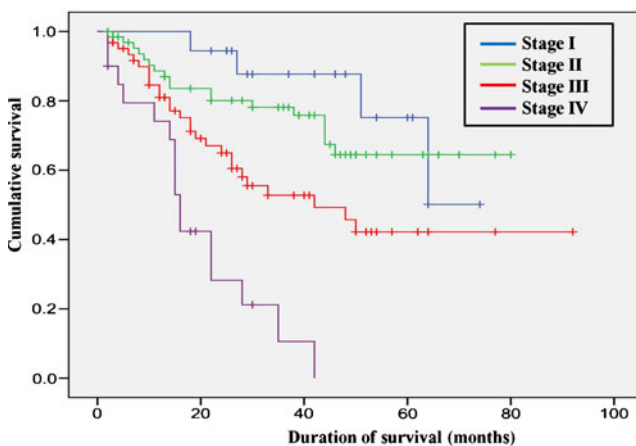
<sup>a</sup>Statistically significant on multivariate analysis

**Table 7** Follow-up data of the 171 patients

Characteristics	Number (percent)
Number of patients who were readmitted upon discharge	128 (74.9)
Total number of readmissions	221 episodes
Median number of readmissions	2 (0–15)
Reason for readmission	
Nonsurgical	135 (61.1)
Surgical	86 (38.9)
Median follow-up, range (months)	27 (2–92)
Recurrent disease	31 (15.2)
Median time to recurrence, range (months)	12 (3–50)
Location of recurrence	
Liver	16 (51.6)
Lung	11 (35.5)
Peritoneum	10 (32.2)
Bone	2 (6.5)
Brain	1 (3.2)
Local recurrence	6 (19.4)
Eventual mortality	70 (34.3)
Cancer-specific mortality	42 (60.0)
Death from other causes	28 (40.0)

(range, 2–50 months). The remaining 28 patients died from a multitude of causations such as pneumonia, urinary tract infection, myocardial infarction, and cerebrovascular accident with a median survival period of 14 months (range, 2–64 months).

The overall mean survival duration for stage I, II, III, and IV diseases were 62.3 months, (95% CI, 53.0–71.7), 60.4 months (95% CI, 52.9–68.0), 51.6 months (median, 42, 41.1–62.1 months), and 19.3 months (median, 16; 95% CI, 13.5–25.2), respectively. Apart from the stage of the malignancy (Fig. 1), the presence of severe complications was also



**Fig. 1** Overall survival curve of patients according to the stage of malignancy ( $p < 0.001$ )

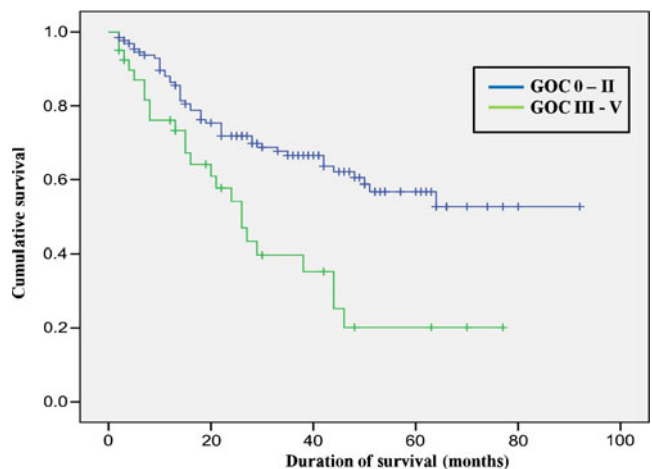
associated with decreased long-term survival (mean of 60.8 months in the group GOC 0–II against 33.0 months in GOC III–IV; Fig. 2). Advanced malignancy and severe perioperative complications were also associated with a poorer disease-free survival (Figs. 3 and 4). Other factors such as age, ASA score, Charlson Comorbidity Index, emergency surgery, and site of disease were not related to survival.

**Discussion**

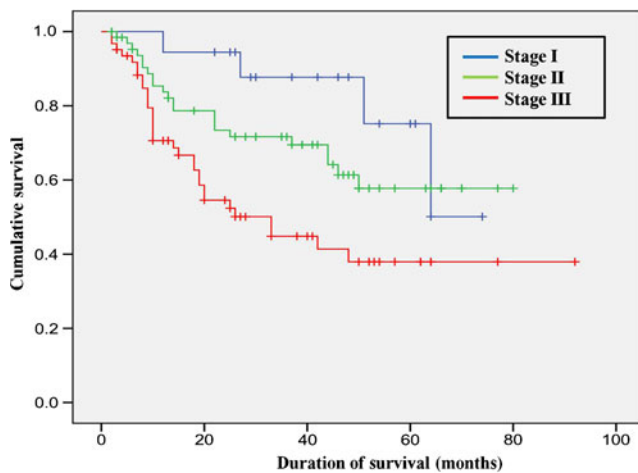
Our series affirmed the significant morbidity and mortality rates associated with surgery for colorectal cancers in octogenarians. Although our 30-day mortality rate of 16.2% is slightly higher than other reports,<sup>4–8</sup> this is likely due to the high proportion of emergency cases (40.7%) seen in our series. Emergency surgery itself has been quoted as an independent factor with worse outcomes in several studies.<sup>12–17</sup>

It has always been more difficult to assess the impact of comorbidity in elderly patients. Indices such as ASA and the number of comorbid conditions are far from ideal. The Charlson Comorbidity Index was adopted in our series as it has been validated in this unique population to be more accurate in ascertaining the impact of the various comorbid conditions and has been shown to be predictive of perioperative complications.<sup>18–20</sup> This was also demonstrated in our series with a higher Charlson Comorbidity Index being associated with worse perioperative outcome. However, we urge caution in the routine adoption of this scoring system in all surgical patients as there is an inherent bias against patients with malignancy and even more so if metastatic disease was present.

From our study, almost half of our patients had a stoma created. This would have contributed to the low rate of anastomotic leak. Of the 96 patients who had a stoma created, 45 underwent a Hartmann’s procedure. Twenty-six



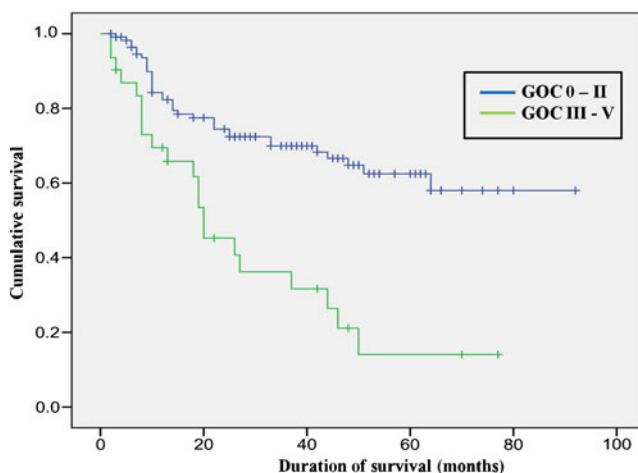
**Fig. 2** Overall survival curve of patients according to the severity of complications ( $p < 0.001$ )



**Fig. 3** Disease-free survival curve of patients according to the stage of malignancy ( $p < 0.001$ )

of them were performed in an emergency setting. In an elective setting, Hartmann's procedure is perhaps applicable in patients who have poor anal tone, high operative risks, or are discouraged to undergo any further operation if a defunctioning stoma would have been created otherwise. Its other advantages include the shorter operative time compared to an anterior resection with defunctioning ileostomy, while the absence of an anastomosis exclude the possibility of an anastomotic leak.<sup>21,22</sup> Unfortunately, these end colostomies often remained permanent.<sup>22,23</sup>

While the stage of the malignancy is a well-known factor associated with survival,<sup>2,3,7</sup> the implications of having worse perioperative complications appears to be far-reaching than anticipated. In our series, the presence of significant postoperative morbidity was associated with disease recurrence and worse overall and disease-free survivals. This has been postulated to be because of the sustained and exaggerated systemic



**Fig. 4** Disease-free survival curve of patients according to the severity of complications ( $p = 0.005$ )

inflammatory responses that may have immunosuppressive implications,<sup>24–26</sup> enabling proliferation of metastatic tumor cells.<sup>24–28</sup> In addition, the impact of these perioperative complications is further compounded in the elderly population who are already laden with numerous comorbidities. The considerable deconditioning from these complications would have predisposed them to further insults from various causations subsequently. It is unlikely that this observation can be attributed to the delay in adjuvant chemotherapy as the majority of our patients did not undergo subsequent chemotherapy anyway. Hence, more effort must be emphasized to reduce perioperative morbidity as it does have long-term implications.<sup>27,28</sup>

Although the disease recurrence rate of 21.2% seen in our series is comparable to other reports,<sup>2,3,7</sup> it would not be surprising if the true rate of disease recurrence in our series is actually higher. This is possibly because of the reluctance of the patients' families or the patients themselves to undergo further postoperative investigations as they may not be keen for subsequent therapies regardless of the findings. In addition, these patients could also die from other nonrelated causations while harboring undiagnosed recurrent disease.

The low rate of the adoption of chemotherapy in our series was not unexpected. This could be due to the hesitancy to initiate chemotherapy from both the patients and the oncologists because the anticipated benefits in extending their survival may not outweigh the potential adverse effects of these medications. Although there is growing evidence supporting the role of adjuvant chemotherapy in elderly patients, careful patient selection is of paramount importance.<sup>29–32</sup> The expected life expectancy, presence of comorbidities, likely treatment tolerance, and patient's preference are important considerations.<sup>29–32</sup>

On a similar note, the aforementioned reasons are likely contributory factors in the fact that none of our patients with rectal cancers underwent neoadjuvant therapy. In addition, neoadjuvant chemoradiotherapy for advanced distal rectal cancer was only adopted in the later part of the study period. Furthermore, some of the proven benefits such as sphincter preservation and improved functional outcomes may not be as applicable in certain elderly patients.

On the other hand, the benefits of neoadjuvant therapy cannot be underestimated in the elderly population. In those with good clinical response, the option of a less extensive surgery such as local excision could be contemplated.<sup>33,34</sup> If complete clinical response following neoadjuvant therapy was seen, there might even be the role of observation in certain selected patients as advocated by Habr-Gama and colleagues.<sup>35,36</sup> However, at this juncture, these options remained controversial.

Although laparoscopic resection has been shown to be safe and beneficial in elderly patients with colorectal cancer,<sup>37–40</sup> the routine adoption of laparoscopy in our institution only began over the past few years. Some of its reported benefits

included fewer perioperative complications, earlier return of bowel movement, reduced pain, and shorter length of hospitalization.<sup>37–40</sup>

As with most studies, there were several limitations in the present one. This series of patients was enrolled from a single institution and its retrospective nature would have masked several other important factors that could be accountable for the outcomes measured. The impact of worse perioperative outcome on the long-term survival merits further evaluation in future studies.

The management of octogenarians with colorectal cancers poses unique problems to surgeons and oncologists alike. Treatment in these patients should not be withheld simply because of their chronological age as long-term survival is possible. However, early stratification based on patients' physiological status may be important to lower the incidence of postoperative complications. In addition, early detection and management of postoperative complications not only lower postoperative morbidity and mortality but could also be oncologically beneficial in the long-term. Neoadjuvant or adjuvant therapy should also not be withheld purely based on their chronological age and be administered on a case by case basis, especially in those patients with good performance status.

## Conclusion

Surgery for octogenarians with colorectal cancers is associated with significant morbidity and mortality rates. Long-term survival is dependent on the stage of the malignancy and the presence of severe perioperative complications.

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